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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/489,711	01/24/2000	David S. Roberts	PC10299A	6167

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EXAMINER	
DEVI, SARVAMANGALA J N	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 10/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/489,711	ROBERTS ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13,14,16,17,24-27 and 30-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,14,16,17,24-27 and 30-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendment

1) Acknowledgment is made of Applicants' amendment filed 08/06/04 in response to the non-final Office Action mailed 04/16/04.

Status of Claims

2) Claims 15 and 28 have been canceled via the amendment filed 08/06/04.

Claims 13 and 17 have been amended via the amendment filed 08/06/04.

New claims 32-39 have been added via the amendment filed 08/06/04.

Claims 13, 16, 17, 24-27 and 30-39 are pending and are under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Moot

5) The rejection of claims 15 and 28 made in paragraph 18 of the Office Action mailed 04/16/04 under 35 U.S.C § 102(b) as being anticipated by Frantz *et al.* (US 5,695,769) as evidenced by Barenholz *et al.* (US 6,156,337), is moot in light of Applicants' cancellation of the claims.

Rejection(s) Withdrawn

6) The rejection of claims 13, 16, 17, 24-27, 30 and 31 made in paragraph 18 of the Office Action mailed 04/16/04 under 35 U.S.C § 102(b) as being anticipated by Frantz *et al.* (US 5,695,769) as evidenced by Barenholz *et al.* (US 6,156,337), is withdrawn in light of Applicants' amendments to the claims and/or the base claim(s).

Response to Applicants' Arguments on Frantz *et al.*

7) Applicants contend that the independent claim 13 has been amended to specify that the *Erysipelothrix rhusiopathiae* fluid fraction is inactivated with beta-propiolactone (BPL).

Applicants submit that Frantz *et al.* do not teach or suggest inactivating the *Erysipelothrix rhusiopathiae* fluid fraction with BPL. Applicants state that those skilled in the art would not have reasonably expected that a BPL-inactivated fluid fraction of *Erysipelothrix rhusiopathiae* would have sufficient immunoprotective effect. Applicants further contend that Frantz *et al.* do not teach a vaccine composition comprising an inactivated *Erysipelothrix rhusiopathiae* fluid fraction and a specific adjuvant.

Applicants' arguments have been carefully considered, but are non-persuasive. It should be noted that independent claims 1, 30 and 34 do not require the *Erysipelothrix rhusiopathiae* culture to be inactivated with beta-propiolactone (BPL). New claims 32 and 37 require the inactivation of *Erysipelothrix rhusiopathiae* culture with formalin. With regard to claim 13, as set forth below under the art rejection(s), the disclosure of Frantz *et al.* anticipates the instant invention, or in the alternative, renders the claimed invention obvious, for the reasons set forth below. Contrary to Applicants' argument, Frantz *et al.* do not have to teach the BPL-inactivated 'fluid fraction' of *Erysipelothrix rhusiopathiae,* because instant claims require the *Erysipelothrix rhusiopathiae* culture, as opposed to the fluid fraction, to be inactivated with BPL. Frantz *et al.* do suggest that BPL can be used as an inactivating agent. Furthermore, since the limitation 'inactivated with beta-propiolactone' is a process limitation in a product claim, claims are not limited to the manipulations of the recited step(s), but only the structure implied by the steps. See below for a detailed reasoning.

Rejection(s) under 35 U.S.C § 112, First Paragraph (New Matter)

8) Claims 24-27, 35 and 36 are rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

There appears to be no descriptive support within the instant specification for the recitations: 'stabilizing agent is aluminum hydroxide' from claims 24, 26 and 35; and 'said stabilizing agent, aluminum hydroxide, is added .... to a final concentration of 30% v/v' from claims 25, 27 and 36. All through the specification, the stabilizing agent that is supported and that is added to a final concentration of 30% v/v is 'aluminum hydroxide gel', but not aluminum

hydroxide, as recited currently in the instant claims. Therefore, the above-identified limitations in claims 24-27, 35 and 36 are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to point to the descriptive support in the specification as filed, for the above-identified limitation(s), or to remove the new matter from the claim(s).

9) Claims 17, 30 and those dependent therefrom are rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 17 and 30 include the limitation: 'about 8% v/v of an amphiphilic surfactant'. However, there appears to be no descriptive support for such a limitation in the instant specification. The descriptive support at lines 26 and 27 on page 7 of the specification is limited to: 'an amphiphilic surfactant at from about 1.5% to about 6% v/v'. Therefore, the above-identified limitation in claims 17 and 30 are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to point to the descriptive support in the specification as filed, for the above-identified limitation(s), or to remove the new matter from the claim(s).

10) Claim 39 is rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

New claim 39 is drawn to a composition comprising an antigen composition comprising the culture fluid fraction from an inactivated *E. rhusiopathiae* culture, a saponin adjuvant, and a

stabilizing agent which is a metal hydroxide, a metal phosphate, an aluminum hydroxide gel, a calcium phosphate gel, a zinc hydroxide/calcium hydroxide gel, or an alum, wherein the composition 'is stable at 2°C to 8°C for at least one year and provides immunity to weaned pigs for six months'. However, there appears to be no descriptive support within the instant specification for a saponin-containing antigen or vaccine composition as recited, which 'is stable at 2°C to 8°C for at least one year and provides immunity to weaned pigs for six months'. On the contrary, the specification describes that a saponin-containing *E. rhusiopathiae* vaccine when given to piglets as per the same regimen used with No. 1 adjuvant, did not protect against development of clinical erysipelas from virulent challenge at 20 weeks following a second vaccination (see page 10, lines 19-21). The duration of protection or immunity for this vaccine is not disclosed, and the data from page 19 of the specification shows that only one of ten pigs immunized with the vaccine in saponin adjuvant was protected. Therefore, the limitations in claim 39 are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to point to the descriptive support in the specification as filed, for the above-identified limitation(s), or to remove the new matter from the claim(s).

Rejection(s) under 35 U.S.C § 102/103

11) Claims 13, 16, 17, 24-27 and 30-39 are rejected under 35 U.S.C § 102(b) as being anticipated by, or in the alternative, under 35 U.S.C § 103(a) as being unpatentable over Frantz *et al.* (US 5,695,769- already of record) as evidenced by Barenholz *et al.* (US 6,156,337 - already of record).

The term 'about' with regard to the percent v/v of the stabilizing agent, or the adjuvant ingredients recited in the instant claims, is interpreted in this rejection as encompassing ± 10.

Frantz *et al.* disclosed a vaccine composition comprising a culture fluid fraction obtained from a formalin-inactivated *Erysipelothrix rhusiopathiae*. The fraction is clarified by centrifugation and therefore is substantially free of cells of *Erysipelothrix rhusiopathiae*. The

fluid antigen fraction is then concentrated by ultrafiltration to a calculated OD of 16.67. See sections 'B. Inactivation of Bacteria' and 'C. Vaccine Fluid Preparation' at the upper half of column 17. The antigen composition further comprises an aluminum hydroxide gel carrier, i.e., REHYDRAGEL or REHYDRAGEL HPA, or calcium phosphate, or alum at a concentration of between 15 and 60% (see lines 55-65 in column 6; paragraph bridging columns 6 and 7; and the first full paragraph in column 7) and a saponin adjuvant (see claim 7; and lines 41-43 in column 5). The antigen composition comprises saline, Drakeol, i.e., lecithin and mineral oil emulsion at various concentrations, and between 0.7% to 3.2% Tween 80 and 0.3% to 1.8% Span. The lecithin and mineral oil emulsion is present at a concentration of 5 to 40%, or 10% (see claims and second full paragraph in column 21), or 8% v/v of amphiphilic surfactant (see the Table in column 19). The *Erysipelothrix rhusiopathiae*-containing vaccine induced best immunity in swine (see Example 11). That aluminum hydroxide in Frantz's composition intrinsically served as a stabilizing agent is inherent from the teachings of Frantz *et al.* in light of what was known in the art. For instance, Barenholz *et al.* taught the dual role of aluminum hydroxide both as an adjuvant and as a stabilizer in microbial vaccines (see column 13, last two lines).

The disclosure of Frantz *et al.* anticipates the instant claims. Barenholz *et al.* is **not** used as a secondary reference in combination with Frantz *et al.*, but rather is used to show that every element of the claimed subject matter is disclosed by Frantz *et al.* See *In re Samour* 197 USPQ 1 (CCPA 1978). The prior art antigenic composition is viewed as the same as the instant composition. Although Frantz *et al.* are silent about the stability of the composition at 2°C to 8°C for at least one year and induction of immunity to weaned pigs for six months, the prior art antigen composition is expected to have the stability at 2°C to 8°C for at least one year and induction of immunity to weaned pigs for six months. The property of stability at 2°C to 8°C for at least one year and induction of immunity to weaned pigs for six months are viewed as uncharacterized inherent functions inseparable from the prior art composition, absent evidence to the contrary. Since the Office does not have the facilities for examining and comparing Applicants' *Erysipelothrix rhusiopathiae* antigenic composition and the vaccine comprising the same with those of the prior art, the burden is on Applicants to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the of the prior

art *Erysipelothrix rhusiopathiae* antigenic composition and the vaccine comprising the same do not possess the same functional characteristics of the claimed *Erysipelothrix rhusiopathiae* antigenic composition and the vaccine comprising the same). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594.

Furthermore, the limitation 'inactivated with beta-propiolactone' is viewed as a process limitation in a product claim. When claims are drawn to a product-by-process, claims are not limited to the manipulations of the recited step(s), but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Applicants have not shown that the alleged difference(s) in the process results in a product that is structurally different from the product of the prior art. In the instant case, Applicants have not shown that the underlying structure of the prior art polypeptide differs from that of the instantly claimed polypeptide.

Alternatively, if one viewed Frantz's disclosure as not being anticipatory, then the instant invention would have been *prima facie* obvious over the prior art of record, because Frantz *et al.* expressly taught that other inactivating agents, such as, betapropiolactone may be used as an alternative inactivating agent to formalin or formaldehyde solution (see the first full paragraph in column 6). Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to inactivate Frantz's *Erysipelothrix rhusiopathiae* culture with the art-known beta-propiolactone inactivating agent to produce the antigen composition and the vaccine of the instant invention, with a reasonable expectation of success, because Frantz *et al.* expressly suggested the use of beta-propiolactone as an alternative inactivating agent to inactivate the culture. Substitution of one inactivating agent with another, art-known, alternative

inactivating agent is well within the realm of routine experimentation, would have been obvious to one of ordinary skill in the art, and would have brought about similar results or effects.

Rejection(s) under 35 U.S.C § 112, Second Paragraph

12) Claims 13, 16, 17, 24-27 and 30-39 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claims 13, 17, 30 and 34 have improper antecedent basis in the limitation: 'the *E. rhusiopathiae* culture is inactivated', because there is no earlier recitation of any *E. rhusiopathiae* 'culture' in the claims.

(b) Analogous criticism applies to claims 32 and 33, which depend from claim 17 or claim 30.

(c) Analogous criticism applies to claims 37 and 38, which depend from claim 34.

(d) Claims 17 and 34 are confusing, grammatically incorrect, and/or inconsistent with the claim language used in claims 13 and 30 in the recitation: 'composition comprises ..... culture fluid fraction and a stabilizing agent, the *E. rhusiopathiae* culture is inactivated ..'. For clarity and consistency, it is suggested that Applicants insert the recitation with: --wherein-- after the recitation 'stabilizing agent',.

(e) In line 1 of claim 16, for clarity and proper antecedence, it is suggested that Applicants replace the recitation 'the fluid fraction' with --the culture fluid fraction--.

(f) Claim 24 lacks proper antecedent basis in the limitation: 'said stabilizing agent is aluminum hydroxide'. Claim 24 depends from claim 13, wherein the scope of the stabilizing agent is limited to 'an aluminum hydroxide gel' as opposed to an 'aluminum hydroxide'.

(g) Analogous criticism applies to claim 25 which depends indirectly from claim 13.

(h) Claims 26 and 27 lack proper antecedent basis in the limitation 'said stabilizing agent is aluminum hydroxide'. Claims 26 and 27 depend from claim 17, wherein the scope of the stabilizing agent is limited to 'an aluminum hydroxide gel' as opposed to an 'aluminum hydroxide'.

(i) Claim 35 lacks proper antecedent basis in the limitation 'said stabilizing agent is aluminum hydroxide'. Claim 35 depends from claim 34, wherein the scope of the stabilizing

agent is limited to 'an aluminum hydroxide gel' as opposed to an 'aluminum hydroxide'.

(j) Analogous criticism applies to claim 36 which depends indirectly from claim 34.

(k) Claims 16, 24-27, 31-33 and 35-39, which depend directly or indirectly from claim 13, 17, 30 or 34, are also rejected as being indefinite because of the indefiniteness identified above in the base claim.

Relevant Prior Art

13) The prior art made of record and not currently relied upon in any of the rejections is considered pertinent to Applicants' disclosure:

- Jones *et al.* (US 5,069,901) disclosed a vaccine comprising a formaldehyde-inactivated *E. rhusiopathiae*, 25% v/v sterile aluminum hydroxide gel and 5% Drakeol™ (see section II in column 17).

Remarks

14) Claims 13, 16, 17, 24-27 and 30-39 stand rejected.

15) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of amendments, responses and paper is (703) 872-9306.

16) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

17) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A telephone message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

October, 2004

S. DEVI, PH.D.
PRIMARY EXAMINER